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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/269,903	05/06/1999	PETER JAMES WATTS	WC131	1775

570 7590 07/12/2005

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EXAMINER	
CHOI, FRANK I	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/269,903	WATTS, PETER JAMES	
	Examiner	Art Unit	
	Frank I. Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-48,51-54 and 58-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-48,51-54 and 58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5/6/1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

8.00

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/2004 has been entered.

Specification

The disclosure is objected to because of the following informalities:

Page 13, line 6: "Figures" should be "Drawings".

Preliminary Amendment (4/2/1999), amending first line of Specification should instead set forth the following:

"This application is a 371 of PCT/GB97/02726, filed on October 6, 1997"

Appropriate correction is required.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 62 been renumbered as claim 61.

Misnumbered claim 63 been renumbered as claim 62.

Drawings

The drawings (5/6/1999) are objected for the reasons set forth in PTO-948 (6/21/1999).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-48, 51-54,58-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising pellets, alkali metal salts of ridogrel and sodium cromoglycate and enteric coating in which the polymer dissolves at a pH values of 4.5 to 8 does not reasonably provide enablement for any thromboxane synthase A2 inhibitors and thromboxane A2/prostaglandin endoperoxide receptor antagonists or the use of any other drug having a free acid group, a pKa in the range of 2.0 to 9.0 which has a higher solubility at a pH 4.5 to 8.0 than a free acid form of the drug, the use of polymers having dissolve pH of greater than 8, or the means to prevent release of the drug which does not include a polymer which dissolves at the appropriate pH. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is directed to compositions and methods wherein a drug having a free acid group, a pKa in the range of 2-9, is present in the composition as an alkali metal salt that has a higher solubility at pH 4.5 to 8.0 than a free acid form the drug is contained in the inner core of a pellet coated with a rate controlling membrane and composition is prepared or formulated to prevent release of the drug until the composition reaches the terminal ileum or colon by use of a polymer which dissolves at a pH of 4.5 or above.

(2) The state of the prior art

The prior art of record appears to use the same materials but do not appear to disclose means other than what is specifically described by Applicant for preventing release of the drug until the composition reaches the terminal ileum or colon. Other than what Applicant has disclosed in the Specification, the prior art of record does not appear to expressly disclose drugs having a free acid group, a pKa in the range of 2-9, in which the alkali metal salt has a higher solubility at ph 4.5 to 8.0 than a free acid form of the drugs.

(3) The relative skill of those in the art

The relative skill of the those in the art is high with respect to the specifically disclosed compounds having the appropriate pH range which are used as means of preventing release of the drug until the composition reaches the terminal ileum or colon. However, in vitro tests are not always predictive of drug absorption in vivo. (See Hardy et al., Drug Delivery to the Gastrointestinal Tract, pgs. 87,88 (dissolving pH of the enteric polymer is critical, too low and the drug is released in the stomach, too high and insufficient drug is released in the small

intestine; for example, shellac, which dissolves at a pH of 7, which Applicant has described as being suitable, due to its high pH solubility failed to provide sufficient drug absorption). Further, Remington's (19th Ed. 1995) indicates that there is no reliable way of predicting the influence of a particular salt species on the behavior of the parent compound in dosage forms (Pg. 1456). Even where many salts of the basic compound have been prepared, there are no effective screening techniques which make the selection process of the salt an easier task for the pharmacist. Id.

(4) The predictability or unpredictability of the art

In light of (2) and (3), the predictability of the art to obtain a suitable salt and dosage form which can administered by the dosage form in the terminal ileum or colon is low.

(5) The breadth of the claims

The claims are very broad. The claims broadly mention a membrane, a polymer which dissolves at a pH of 4.5 or above and any drug having a free acid group, a pKa in the range of 2-9, in which the alkali metal salt has a higher solubility at ph 4.5 to 8.0 than a free acid form of the drugs, of which a subgenus includes said drugs which are thromboxane synthase A2 inhibitors and thromboxane A2/prostaglandin endoperoxide receptor antagonists. Further, claims 42, 43, 44, 48 and 60 recites a "means" in which does not require the presence of a polymer which dissolves at the appropriate pH.

(6) The amount of direction or guidance presented

The only drugs specifically described are ridogrel and sodium cromoglycate. The possible drugs are either described by function or by the claimed chemical characteristics, for example thromboxane synthase A2 inhibitors thromboxan A2/prostaglandin endoperoxide receptor antagonsists. The specification does not appear the indicate what other drugs would be

suitable for treatment of ulcerative colitis, Crohn's disease, irritable bowel syndrome or inflammatory bowel disease or the appropriate dose of these undisclosed drugs. The only means disclosed in the Specification appears to require the presence of a polymer which dissolves at an appropriate pH. See In re Dreshfield, 45 USPQ 36 (CCPA 1940) ("It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 140 USPQ 471; In re Barr et al. (CCPA 1971) 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification provides limited examples of specified drugs and means of preventing release of the drug until the composition reaches the terminal ileum or colon.

(8) The quantity of experimentation necessary

In light of the above, it appears that one of ordinary skill in the art would be required to do undue experimentation in order to determine suitable drugs for treatment of the claimed diseases/conditions, drugs which act as thromboxane synthase A2 inhibitors thromboxan A2/prostaglandin endoperoxide receptor antagonsists which also contain contain a free acid group, and which of said drugs or other drugs have a pKa in the range of 2-9 and which can form an alkali metal salt which has a higher solubility at a pH 4.5-8 than the free acid form of the

drug, an which alkali metal salt will not have an adverse effect on the activity of the parent drug, to determine suitable polymers which will dissolve at the appropriate pH when in part of the formulation such that the coating made from said polymer will prevent release until the terminal ileum or colon but not prevent absorption of the drug from reaching therapeutic levels, and to determine what other means would prevent said release but not prevent absorption of the drug.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required to establish enablement. In re Fisher, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

Contrary to Applicant, the advisory action did not confirm that the amendments were sufficient to overcome the rejection. The Advisory Action (4/1/2004) specifically indicated that the pH range of 4.6 or above was not enabled because (4/1/2004) the range include polymers which dissolve at a pH greater than the pH range of the colon. Further, as indicated above, even polymers which have a pH of 7 have been shown to result in subtherapeutic or no levels of drug after administration of the enteric-coated dosage form. With respect to the rejection of the "means", claims 42, 43, 48 and 60 still claim a means without requiring the presence of a polymer which dissolves at the appropriate pH.

Applicant's submits the declaration of the inventor, however, said affidavit is insufficient to overcome the rejection herein. The fact that it is within the skill of one of ordinary skill to determine whether a given compound is a drug, to determine pH and pKa and to form salts of drugs does not enable the entire scope of Applicant's claimed invention. In the first instance,

Applicant's claims are not limited simply to drugs which may be found in the US Pharmacopoeia, the claim includes any compound having the claimed chemical characteristics which must be tested to determine if it constitutes a drug or more specifically whether it will effective for the claimed diseases or will act as thromboxane synthase A2 inhibitors thromboxan A2/prostaglandin endoperoxide receptor antagonsist. As indicated in Remington's, there is no reliable way to predict how the salt form will effect the activity of the parent drug in the dosage form. Pharacoscinitgraphy is used to test a given formulation to determine whether it will deliver to the appropriate site in the intestine. It does not appear that it can predict how other formulations will behave absent actually testing said formulations. The issue it not whether a given formulation works, the issue is whether from a given species or limited number of species, one of ordinary skill in the art could reasonably predict without undue experimentation that the genus would also behave similarly. The fact that Hardy et al. was published in 1989 and discusses an outdated disintegration test does not overcome the rejection herein. This does not overcome the fact that the dissolution pH of a given polymer can exceed the pH range of the colon and therefore the formulation will not deliver any drug in the colon and that the fact that a salt can be prepared is not predictive of whether the salt will be suitable for the dosage form or be therapeutically effective. Applicant argues that the actual release profile of the present invention has been shown by in vivo tests, however, said in vivo tests are limited to a specific formulation. There is no showing that the specific formulation is sufficiently predictive of the entire scope of the claimed invention. As such, in light of the breadth of the claims and the unpredictability of the art in relation to enteric coated dosage forms and the activity of salts in a given dosage form, it appears that undue experimentation would be required.

Claims 42, 43, 45, 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as follows:

Claims 42, 43 recite the limitation "means". There is insufficient antecedent basis for this limitation in the claim in that claim 58 does not recite "means."

Claim 45 recites a ratio of 100:0 of two polymers, i.e. claim 44 contains only one of the polymers, which renders the claim indefinite as claim 44 on which the claim is dependent requires the presence of both polymers.

Claim 48 is dependent on cancelled claimed 29.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32, 36, 37,40, 51-54,58-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Dansereau et al. (US Pat. 5,622,721).

Dansereau et al. expressly discloses risedronate sodium-coated beads prepared by coating risdronate sodium and HPMC and PEG on sugar sphere, 20-25 mesh, which beads are then coated with Eudragit L-30 D ®, which enteric coated beads are encapsulated in a hard shell gelatin capsule (Column 15, lines 9-68, column 16, lines 1-15) falling within the scope of applicant's claims. See In re Fitzgerald, 205 USPQ 594 (CCPA 1980). See also In re May, 197 USPQ 601, 607 (CCPA 1978). See also Ex parte Novitski, 26 USPQ2d 1389, 1390-91 (Bd Pat. App. & Inter. 1993).

Claims 30, 32-48, 51-54,58-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 1017674 in view of The Merck Index (1989), Schreiber et al., Ligumsky et al., Eichel et al. (US Pat. 5,376,384), Rhodes et al. (US Pat. 5,541,170), Kelm et al. (US Pat. 5,686,106) and Chambers (US Pat. 4,211,777).

GB 1017674 discloses a coated pharmaceutical composition, in the form of a granulate, containing sodium or calcium acetyl-salicylate or sodium or calcium p-amino-salicylate which prevents release of alkali metal salicylate until the colon in which the granulate is coated with a layer of a basic amino-containing polyelectrolyte which is resistant to both alkali and intestinal juice and soluble in acid, a lather of a hydrophilic substance and a layer of a carboxyl-containing polyelectrolyte which is resistant to acid and to gastric juice falling (Page 1, lines 9-20, Page 3, lines 83-125, Claims 4, 8). It is disclosed that the layer comprising the substance which is acid soluble and resistant to intestinal juice remains intact and is semi-permeable, as such, if the active agent is water-soluble, the active agent will very slowly be released from the composition; which release rate can be regulated as desired (Pg. 2, lines 86-127). It is disclosed that examples of coatings resistant to intestinal juices include cellulose derivatives, such as methyl cellulose, polyacrylates or polymethyacrylates (Pg. 3, lines 101-124).

The Merck Index discloses that the pKa of p-aminosalicylic acid is 3.25, that the pH of a 0.1% aqueous solution is 3.5 and that 1 gram dissolves in about 500 ml of water, whereas 1 gram of the sodium salt dissolves in 2 ml water and 1 gram of the calcium salt dissolves in about 7 ml of water, and that the pH of a 1% solution of the sodium salt is 7 (Pg. 78) It is disclosed that the pKa of aspirin is 3.49 and that 1 gram dissolves in 100 ml water at 37 degrees Celsius, whereas 1 gram of the calcium salt dissolves in 6 ml of water (Pgs. 134, 250).

Schreiber et al. discloses that para-aminosalicylic acid is effective in the treatment of Crohn's disease and ulcerative colitis comparable to 5-aminosalicylic acid (5-ASA) and that the sodium salt of para-aminosalicylic acid is more stable than 5-ASA (Pg. 1081).

Ligumsky et al. discloses that aspirin and 5-ASA inhibit the production of thromboxane A2 which may be involved in the inflammatory response in ulcerative colitis (Pg. 444).

Eichel et al. disclose that the maximum time of effectiveness in many pharmaceutical preparation, particularly those containing a drug such as aspirin, is only a few hours because of biological modification and/or elimination which requires repeated doses at frequent intervals t obtain longterm therapeutic levels of drug (Column 1, lines 13-21). It is disclosed that these drugs usually dissolve readily in digestive juices and the total dosage is immediately fed into the blood stream which results in a initial high peak which constantly decreases such that there is little or no therapeutic effect at the end of the period between doses resulting in peaks and valley in the level of the drug in the blood (Column 1, lines 21-30). It is disclosed that the core drug is preferably a water soluble drug having a solubility of greater than approximately 10 grams per liter in intestinal fluid which may be coated on sugar spheres or formulated to produce core drug granules, preferably having a size range from about 500 to 1500 microns (Column 4, lines 57-

68). It is disclosed that the coating of the core preferably includes Eudragit NE30D or ethyl cellulose (Column 4, lines 3-16, Column 5, lines 1-7).

Rhodes et al. disclose that in the treatment of diseases or ailments of the colon or rectum administration of the pharmacologically active agent, such as 5-amino-salicylic acid which is used to treat colitis and Crohn's disease, to the affected site may be required (Column 1, lines 10-34, Column 2, lines 51-64). It is disclosed that anionic polymers have been known for many years to be of use in the preparation of coatings for tablets and other oral dosage forms to provide delayed or sustained release of the active agent and that since at least 1974 It has been known to use anionic copolymers of methy-acrylic acid and methacrylic acid methyl ester such as Eudragit® S which is insoluble in gastric juice and poorly soluble in intestinal juice and dissolves in a pH above 7 and Eudragit ® L which is insoluble in gastric juice and readily soluble in intestinal juice (Column 2, lines 26-45). It is disclosed that anionic polymer coatings on oral dosage forms have been required to dissolve in aqueous medium usually between pH 5.5 and pH 7 and that although Eudragit ® dissolves above pH 7 it is usually employed as an admixture with Eudragit ® L and which mixture dissolves below pH 7 (Column 2, lines 45-50).

Kelm et al. disclose a unit dosage form for containing a therapeutic agent useful for topical treatment of diseases of the colon such as irritable bowel syndrome, Crohn's disease and ulcerative colitits, including nonsteroidal anti-inflammatory drugs, such as 5-aminosalicylic acid (Column 6, lines 5-12, 15). It is disclosed that the therapeutic agent is incorporated into or coated on the surface of a spherical substrate, such as a sugar sphere, a hard capsule, such as a starch capsule or a compressed tablet (Column 7 lines 20-68, Column 8, lines 1-60). It is disclosed that the enteric polymer coating prevents the release of the therapeutic agent until the

dosage form reaches the junction between the small intestine and the colon or is in the colon, and includes such polymers as Eudragit ® L (Column 8, lines 61-68, columns 9, 10).

Chambers discloses that aminosalicylic acids and there salts have been used in mammals mainly for treatment of tuberculosis and that the side effects of the same can be reduced by combination with disodium cromoglycate like compounds (Column 1, lines 8-19). It is disclosed that the composition can be formulated in sustained or controlled release form by coating granules of drug particles with semi-permeable membranes (Column 5, lines 13-24). It is disclosed that the combination can be used to treat Crohn's disease, ulcerative colitis and irritable bowel syndrome (Column 3, lines 65-68, Column 4, lines 1, 2). It is disclosed that coated granules may in the form of a capsule or tablet containing the granules which can be enteric coated to make the drugs available at the appropriate part of the gastrointestinal tract (Column 5, lines 24-36).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose at least one pellet comprising an inner core coated with a rate-controlling membrane and the inner core comprises a salt of a drug and a coating of a polymer that dissolves at pH 4.5 or above for preventing the release of the drug until the composition reaches the terminal ileum or the colon coating the pellet or a dosage form containing said pellet, and the drug has a free acid group, a pKa in the range of 2.0 to 9.0 and is present in the composition as an alkali metal salt that has a higher solubility at pH 4.5 to 8.0 than a free acid form of the drug, a method of making said pellet with both the membrane and pH dissolving coating, a method of improving the controlled release profile of a drug said pellet with both the membrane and pH dissolving coating by administering said pellet and a method for treatment of ulcerative colitis, Crohn's disease, irritable bowel syndrome and inflammatory bowel disease by administering said

pellet containing a suitable drug effective for the same in said pellet both the membrane and pH dissolving coating. However, the prior art amply suggests the same as the prior art discloses a granule which is coated with a semipermeable membrane and enteric coating and containing an alkali metal salt of p-aminosalicylic acid (p-ASA), that p-ASA is effective for treatment of Crohn's disease and ulcerative colitis, that p-ASA has a pKa of 3.25 and that the calcium salt is greater than ten time more soluble that the free acid form and that the sodium salt is greater than 100 times more soluble that the free acid form of p-ASA, that the rate-controlling membrane can contain methacrylate copolymer or ethylcellulose, that the inner core can be in the form of a sugar sphere in which the salt is coated theron, that the granules can contained in a starch capsule or compressed tablet coated with polymethacrylate, such as mixtures of Eudragit ® L and Eudragit ® S, to prevent release until the terminal ileum or colon. As such, it would have been well within the skill of an one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the alkali salt form the drug would be suitable for extended release and absorption of the drug in the terminal ileum and colon, that the semi-permeable membrane would permit a constant extended release avoiding the need for multiple doses over short intervals and peaks and valleys in the amount of drug between doses, that the enteric coating on the pellet or dosage form in which the pellet is contained would permit selective delivery to the colon or terminal ileum of the aspirin or aminosalicylic acid for treatment of such diseases as Crohn's disease and ulcerative colitis.

Examiner has duly considered Applicant's arguments but deems them unpersuasive in light of the new grounds of rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

FIC
July 9, 2005

SABIHA QAZI, PH.D
PRIMARY EXAMINER